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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/665,005	09/19/2003	Kamil Paruch	OC01625K	5836

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SCHERING-PLOUGH CORPORATION
PATENT DEPARTMENT (K-6-1, 1990)
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EXAMINER

RAO, DEEPAK R

ART UNIT

PAPER NUMBER

1624

DATE MAILED: 11/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/665,005	Applicant(s) PARUCH ET AL.	
	Examiner Deepak Rao	Art Unit 1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 16 September 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,2,5-8,10-12,17-19 and 25-29 ~~is~~ are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 18 is/~~are~~ allowed.
- 6) ☒ Claim(s) 1-2, 5-8, 10-12, 17, 19, 25-29 ~~is~~ are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

This office action is in response to the amendment filed on September 16, 2004.

Claims 1-2, 5-8, 10-12, 17-19 and 25-29 are pending in this application.

Withdrawn Rejections/Objections:

Applicant is notified that any outstanding rejection/objection that is not expressly maintained in this office action has been withdrawn or rendered moot in view of applicant's amendments and/or remarks.

The following rejections are maintained:

Claims 1-2, 5-8, 10-12, 17, 19 and 25-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Burns et al., WO 02/60492, for the reasons of record which are incorporated here by reference.

Applicant's arguments have been fully considered but they were not deemed to be persuasive. Applicant first argues that the 'instantly claimed compounds are structurally dissimilar from the teaching of the '492 publication and the instant structures or synthesis are not taught by the reference'. Contrary to applicant's assertion, the reference teaches imidazo[1,2-a]pyrazine compounds (see formula II in page 10) which is structurally analogous to the instantly claimed compounds and further, teaches a method of synthesis of the compounds, see Scheme 2 in page 25. The reference further discloses a compound within the genus of formula II, see compound 57 (page 56, last compound). As indicated in the previous office action(s), the only structural difference between the instantly claimed compounds and the reference compounds is

Art Unit: 1624

the presence of substituent R^2 in the instantly claimed structural formula as compared to the reference compound which is unsubstituted at the analogous position. The claims recite that R^2 can be alkyl, e.g., methyl and thus, the instant compounds differ from the reference compounds by a $-CH_2$ group and therefore are homologs of the reference compounds.

Applicant next argues that 'even a simple homolog change, can drastically, significantly and unpredictably change the biological activity' and provides three references (Exhibits C, D and E) which applicant believes as analogous art. However, the references are related to compounds having very different structural nuclei, as compared to the claimed compounds and the reference compounds both of which are drawn to imidazo[1,2-a]pyrazine compounds. For example, Exhibit C is related to pyrrolotriazine compounds; Exhibit D is drawn to pyrido[3,4-d]pyrimidines; and Exhibit E deals with purine compounds. However, objective evidence of nonobviousness must be attributable to the claimed invention.

Based on the various data in each of the exhibits, applicant argues that 'there is lack of predictability or correlation between structural changes'. Applicant provides that Exhibit C shows a drop in biological activity for a H-containing compound (13) to the corresponding methyl compound (16) and Exhibit D shows an increase in activity for H-containing compound (6b) to a methyl compound (9b). However, contrary to applicant's arguments, each of the reference also show compounds having similar properties or compounds with no significant difference in biological activity when the substituent is varied from H to methyl, see e.g., Exhibit C, Table 1, compounds 9 and 10 which represent H vs. methyl variation and show no significant difference in the biological activity. Also, in Exhibit D, compounds 5b and 5c which only vary by a methyl group, display no significant difference in the biological activity.

Art Unit: 1624

The discussion based on the data of Exhibits submitted is particularly not on point because it does not involve compounds having the same core as of the instant claims. Applicant has not provided any evidence or showing that one of ordinary skill in the art would not expect similar properties for the instantly claimed imidazo[1,2-a]pyrazine compounds over the reference disclosed imidazo[1,2-a]pyrazine compounds. Applicant submission on record that 'there is lack of predictability or correlation between even minor structural changes', is contradicting the instant disclosure of thousands of compounds encompassed by the claimed genus, having different structural features, all of which are disclosed to share the same properties, i.e., as protein kinase inhibitors.

The reference teaches imidazo[1,2-a]pyrazine compounds useful as pharmaceutical therapeutic agents, and therefore, the reference provides sufficient motivation to one of ordinary skill in the art to prepare the compounds such as those of the instant claims which differ from the reference compounds by having a ring substituent R^2 , which can be alkyl, e.g., methyl. The skilled chemist would have the reasonable expectation of obtaining compounds with similar properties, absent an evidence of unexpected results.

The following rejection is necessitated by the amendment:

Claim 25 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 25 recites the limitation "treatment" in line 3. There is insufficient antecedent basis for this limitation in the claim. The claim in line 1 recites 'a method of

Art Unit: 1624

inhibiting' and therefore, replacing the above term with -- inhibition -- would obviate the rejection. (This is consistent with claim 19)

Allowable Subject Matter

Claim 18 is allowed. The references of record do not teach or fairly suggest the instantly claimed compounds.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a).

Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deepak Rao whose telephone number is (571) 272-0672. The examiner can normally be reached on Tuesday-Friday from 6:30am to 5:00pm.

Art Unit: 1624

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Mukund Shah, can be reached on (571) 262-0674. If you are unable to reach Dr. Shah within a 24 hour period, please contact James O. Wilson, Acting-SPE of 1624 at (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Deepak Rao
Primary Examiner
Art Unit 1624

November 24, 2004